COURAGE Chronicle

May 2000

Effects of Crossovers on the Interpretation of the COURAGE Trial

Historically in clinical trials there has been a great deal of concern over the effect of crossovers on the interpretation of results. Thus, in the Coronary Artery Surgery Study, surgeons often voiced concern that the high rate of crossovers from medicine to surgery showed that surgery was really the better therapy, and that the crossovers invalidated the trial. This view receded as the clinical community has become more comfortable with the notion of intention-to-treat. Thus, the question becomes not what is the better therapy, but what is the better choice at the moment. From this point of view, the question in the COURAGE Trial is not necessarily whether intervention plus the best possible medical therapy compared to the same medical therapy alone is better in the long run or not, but rather what is the correct decision at the present time. From this vantage point, with a more narrowly defined question, crossovers would appear to be less of a problem. However, this is also a too limited point of view. If patients are allowed to be crossed over too easily from medical therapy alone to PCI plus medical therapy, then no question is really being tested and to the extent that this happens, the results of the trial will become less meaningful. In the extreme, if all medicine-only patients cross over to PCI very rapidly, then the trial will be meaningless. For this reason, the trial leadership has developed quite specific criteria for crossing patients over. Given that the trial is in equipoise, and that we really do not know which arm is better, having explicit criteria for crossovers is **both ethical and in keeping with good clinical trial design.** We urge all investigators to take seriously the issues of when to cross patients over, and to not compromise the trial by ***inappropriately*** crossing patients from Medicine Only to the PCI plus Medicine arm.

Changes to the Operations Manual

As a result of the recent Data Monitoring Board recommendations we are instituting the following changes to the Operations Manual effective immediately:

1. **The window to document objective evidence of myocardial ischemia has been *increased from 90 days to 180 days (six months) before the date of randomization* if there have been no intervening events.**
2. **For patients who present to the hospital with an acute coronary syndrome with classic ("definite") angina, but no diagnostic ischemic ECG changes, if they can be cooled down it will be permissible to enroll them in the study *without* objective evidence of ischemia under the following conditions:**
   - **Patients must demonstrate a COURAGE eligible vessel (see pp. 30-34 of the Protocol) with a lesion that is caliper-measured at = 80% coronary stenosis.**
   - **All other inclusion and exclusion criteria must be met.**

   The use of IIb/IIIa inhibitors should be encouraged in these patients.

These changes in study procedures as outlined in Operations Memos No. 21 and No. 22 will facilitate the ease of screening and enrolling patients into the COURAGE Trial while conforming to current practice.

The Care and Feeding of your Pentablet.

The Pentablet can be a wonderful time saver (the patients can usually complete the questions themselves after being shown how it works, and that means seven less CRFs to fill out) and an effective way to ensure the quality of the data (less chance for transcription errors). At times, however, the Pentablet can be unnecessarily slow. It's operations can be speeded up by leaving it plugged in while the patient is responding to the questions (i.e., keep it well fed). It may also help to scan and defragment (i.e., take care of) the hard disk of your Pentablet. The ScanDisk and Disk Defragmenter are accessories available in *Windows 95*. From the **Start** menu, go to **Programs,** then to **Accessories,** and finally to **System Tools.** Do **ScanDisk** first, then **Disk Defragmenter**. The Disk Defragmenter may be a lengthy process depending on how fragmented your hard disk is. You might start defragmentation at the end of the day and leave it on overnight.

CRFs

By now you should have received all of the printed CRFs. When you need to reorder, please send a Supply Request Form (OPS Manual, p. 12-7) to West Haven, allowing sufficient time for shipment.

PATIENT ENROLLMENT UPDATE

		To Date	Since Annual Meeting
671	Audie L. Murphy VAMC – San Antonio	50	15
202	London Health Sciences Centres	33	17
580	Houston VA Medical Center	30	10
203	Montreal Heart Institute	29	17
506	Ann Arbor VA Medical Center	28	6
È	***WEEK 46: TARGET ENROLLMENT per SITE:***	***27***	***10***
558	Durham VA Medical Center	21	3
209	Sunnybrook & Women's College HSC	17	11
598	John C. McClellan VA – Little Rock	17	8
205	Queen Elizabeth II HSC	16	12
200	Foothills Hospital	16	10
596	Lexington VA Medical Center	16	8
308	Mid America Heart Institute/Shawnee Mission	16	4
630	New York VA Medical Center	15	11
306	Mayo Clinic—Rochester	15	8
584	Iowa City VAMC/Univ. of Iowa Hospital	13	9
663	Seattle VA Medical Center	13	5
312	University of Michigan Medical Center	10	5
313	University of Oklahoma	10	5
304	Emory University Hospital	10	4
301	Albuquerque VA Medical Center	10	3
211	University of Alberta Hospital	9	6
210	The Toronto Hospital	9	2
626	Nashville VA Medical Center	8	4
508	Atlanta VA Medical Center	8	4
301	Boston Medical Center	6	4
207	St. Paul's Hospital	6	4
311	SUNY Health Science Center at Syracuse	5	0
204	St. Michael's Hospital	4	4
208	Sudbury Memorial Hospital	4	3
201	Hamilton General Hospital, McMaster Clinic	4	1
302	Cleveland Clinic	4	0
212	Vancouver Hospital & Health Science Center	3	3
300	Barnes-Jewish Hospital	3	2
314	MIMA Century Research Associate s	2	2
626	Vanderbilt University Medical Center	2	2
307	Christiana Care Health Systems	1	0

Total Patients as of 05/12/2000: 463

Pre-Randomization Meds

Record the medications your patient is taking before being randomized into the study on FORM 9, using 00 as the Visit Sequence number. Use a second FORM 9 with a Visit Sequence number 01 for the medication prescribed for the patient upon entering the COURAGE Trial.

Mail Your CRFs to West Haven

All sites are now asked to use the mail for sending in their CRFs and ECGs. It is imperative that a FIRST CLASS stamp or sticker be clearly visible on the front of the envelope. Please continue to use FedEx for: (1) CDs/cines, catheter tips and the accompanying forms for the Angiographic Core Lab; (2) any Nuclear Imaging data contained on disks; and (3) the blood samples for the Lipid Core Lab. These latter shipments should be sent monthly, no later than Wednesday noon of the week in which they are sent.